

Case Report

A Case of Cerebral Aneurysmal Subarachnoid Hemorrhage in Fabry's Disease

Youn Hyuk Chang, M.D., Sung-Kyun Hwang, M.D.

Department of Neurosurgery, College of Medicine, Ewha Womans University, Seoul, Korea

We report an unusual case of cerebral aneurysmal subarachnoid hemorrhage (SAH) with Fabry's disease. A 42-year-old woman presented with aneurysmal SAH originated from a saccular aneurysm of the right posterior communicating artery. The patient was treated by an endovascular coil embolization of aneurysm. Postoperatively the patient recovered favorably without any neurological deficit. During her admission, the patient had a sign of proteinuria in urine analysis. The pathologic findings of kidney needle biopsy implied nephrosialidosis (mucolipidosis of lysosomal storage disease), which is consistent with a Fabry's disease. It is uncommon that Fabry's disease is presented with aneurysmal SAH, especially in middle-aged patients, but could be a clinical concern. Further investigations are needed to reveal risk factors, vascular anatomy, and causative mechanisms of Fabry's disease with aneurysmal SAH.

Key Words : Fabry's disease · Subarachnoid hemorrhage · Cerebral aneurysm.

INTRODUCTION

Fabry's disease is an X-linked lysosomal storage disorder caused by mutation of the gene that encodes an enzyme alpha-galactosidase A, a mutation inducing accumulation of glycosphingolipids in lysosome, especially in vascular endothelial and smooth-muscle cells¹⁻¹⁷. Patients with the disease commonly have a cerebral vasculopathy causing premature ischemic stroke, usually in the vertebrobasilar circulation. Its prevalence was reported to be high as 4.9% in men and 2.4% in women¹⁵, but hemorrhagic stroke especially in middle-aged patients with Fabry's disease is sufficiently rare¹³. We report an unusual case of cerebral aneurysmal rupture resulting in a subarachnoid hemorrhage (SAH) with Fabry's disease.

CASE REPORT

A 42-year-old woman, who had no previous medical history experienced the sudden onset of severe headache and followed by loss of consciousness. A computed tomography revealed that subarachnoid hemorrhage was located in the basal cistern. Cerebral angiography on the day of admission demonstrated a sac-

cular aneurysm of the right posterior communicating artery (Fig. 1). The aneurysm was treated by an endovascular coil embolization (Fig. 2). Postoperative computed tomography revealed the resolved subarachnoid hemorrhage without posthemorrhagic hydrocephalus and infarction. The patient recovered favorably without any neurological deficit. During her admission, she showed proteinuria in urine analysis. In kidney needle biopsy, the pathologic findings implied nephrosialidosis (mucolipidosis of lysosomal storage disease) consistent of Fabry's disease (Fig. 3). The patient was transferred to the department of nephrology, where she was treated with a gene therapy and medical management. The patient recovered favorably, discharged without any neurological residual symptom.

DISCUSSION

Estimates on the prevalence of classic Fabry's disease are varied from 1 in 40000 to 1 in 11700¹¹, a variation that indicates the patients are frequently misdiagnosed and spend years or even decades receiving inappropriate treatment. A study of 721 patients with cryptogenic stroke, aged 18-55 years, showed a high prevalence of Fabry's disease : 5% (21/432) of men and 3%

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• Address for reprints : Sung-Kyun Hwang, M.D.

Department of Neurosurgery, Ewha Womans University, Mokdong Hospital, 1071 Anyangcheon-ro, Yangcheon-gu, Seoul 158-710, Korea
Tel : +82-2-2650-2872, Fax : +82-2-2650-2652, E-mail : nshsg@ewha.ac.kr

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(7/289) of women¹⁵⁾. In a Belgian Fabry study to investigate prevalence of Fabry's disease, 49 patients (4.9%) were found to have intracranial hemorrhage in a cohort of 1000 young patients with cerebrovascular disease. Meanwhile, 16 patients with intracranial cerebral hemorrhage had a SAH⁴⁾, and 15 were found to have cerebral aneurysm in the same study but they were not associated with aneurysmal rupture as SAH^{4,15)}. The frequency of stroke in men aged 25-44 years can be up to 12 times more frequent than that is expected in the general population while women can have nearly 10 times higher prevalence of stroke when compared to normal women older than 18 years. Renal and cardiac diseases are more frequently seen in patients with cerebrovascular disease¹⁷⁾.

Because Fabry's disease is an X-linked disorder, female patients are regarded as carriers of mild feature of the disease at worst, but there are researches showing a high frequency of cerebrovascular events in woman. Such findings may imply that cerebrovascular involvement at least in a subgroup of clinically affected female patients could be as severe as in hemizygous male patients⁹⁾. Male hemizygotes with this disease are generally more severely affected than heterozygote females, but disabling clinical features and disease progression are what female patients often undergo^{6,10)}. Meanwhile, ischemic strokes with no specific cause are judged to be cryptogenic one, which is more common in younger rather than older patients. Thus, Fabry's disease should be considered in all cases of unexplained stroke in younger patients, especially in cases with combination of cerebral stroke in the vertebrobasilar artery system and proteinuria^{15,17)}.

Although the mechanism linking glycolipid accumulation to cerebral stroke in Fabry's disease has been poorly understood, cerebral microangiopathy may be a hallmark of the disease, implying that lipid deposit in the vascular endothelial and the smooth muscle cells cause oxidative stress, vascular dysfunction, vessel occlusion, and tissue ischemia^{2,8,9)}. These pathological mechanisms are associated with increased risk of premature strokes, progressive white matter lesions, and dolichoectasia. Cerebral stroke frequently occurs before Fabry's disease is diagnosed and other key signs of the disease are found^{12,16,17)}.

As for Fabry's disease, ischemic stroke occurs more frequently than hemorrhagic stroke and can be a consequence of cardiac embolism or cerebral vasculopathy. Sims et al.¹⁶⁾ reported that most patients of the disease had ischemic stroke (105 of 121, 86.8%) and 13 of 77 males (16.9%) and 3 of 44 female (6.9%) experienced hemorrhagic stroke, for which specific stroke type was not described. Hemorrhagic stroke can be a consequence of hypertension secondary to chronic renal failure or weakening of vessel walls due to lipid deposition. Meanwhile, none of the patients exhibited intracranial hemorrhage within the vertebrobasilar region^{3,8,9,16)}. Reisin et al.¹⁴⁾ reported that 44.4% (16 of 46) adult patients without clinical history of cerebral stroke or prior dialysis had evidence of small vessel disease and 11% (5 of 46) showed cerebral micro-bleeding on magnetic resonance image⁵⁾.

CONCLUSION

Fabry's disease is uncommon but requires clinical concern. The disease is frequently associated with ischemic

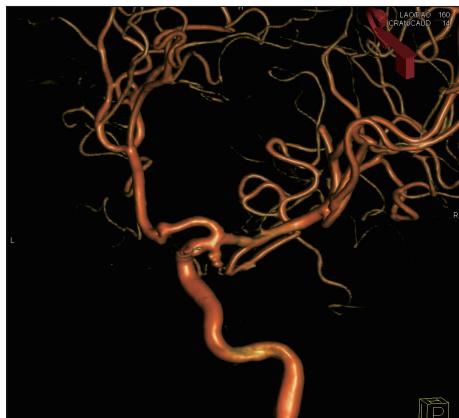


Fig. 1. The preoperative right internal carotid artery angiography showing typical saccular aneurysm of the posterior communicating artery.



Fig. 2. Anteroposterior view of postembolization right internal carotid artery angiography demonstrating complete occlusion of aneurysm preserving a posterior communicating artery.

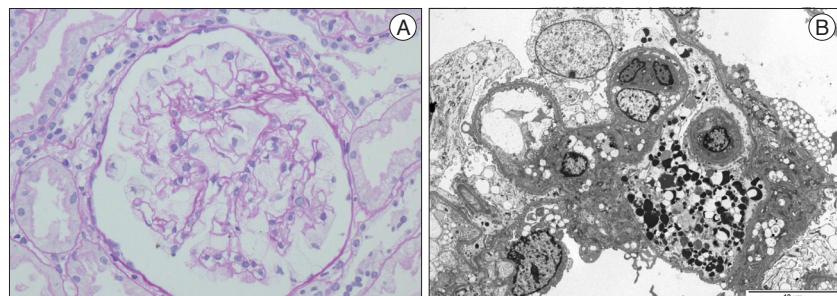


Fig. 3. A : Pathologic findings from light microscopy; all glomeruli show marked swelling of podocyte with expanded foamy or vacuolar cytoplasmic change. Capillary loops of glomeruli are partly collapsed by swollen podocytes. B : Electron microscopy; the ultrastructure of glomerulus show marked expansion of podocytes with severe vacuolar change. Vacuoles have some lipid droplets or watery silk material. Foot process of podocytes is markedly effaced.

strokes, but hemorrhagic strokes such as an aneurysmal rupture to be SAH is rare, especially in middle-aged patients. Further investigation is needed to reveal risk factors, vascular anatomy, and causative mechanisms. In addition, studies with larger cohorts of high-risk patients may help to formulate definite answers for the disease.

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